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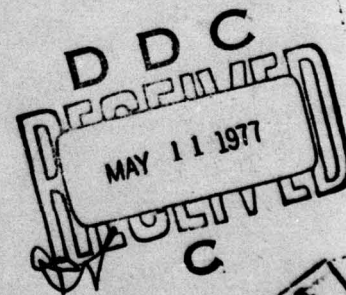
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THE BEHAVIOR OF HEMOLABYRINTHINE, LIQUOR AND
OPHTHALMIC BARRIERS IN ALBINISM

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P. Bonaccorsi**

(Otorhinolaryngological Clinic of the University of
Pavia. Director: Prof. M. Cherubino)

SUMMARY

Albino rabbits were used to study the possible changes occurring in the permeability to sodium fluorescein of hemolabyrinthine, liquor and ophthalmic barriers. These are well known both in human as well as in animal species in albinism-associated congenital pathological phenomena specially localized to the visual, auditory and nervous systems.

After describing albinism from the phenotypical and genotypical standpoint, the author discusses methods, experimental techniques and results. The analysis of the values of fluorescein concentration found in albinos in liquor, aqueous and vitreous humor, perilymph and endolymph showed a lesser permeability of the three barriers to the dye and a delay in its elimination from the liquor systems examined. The author suggests an interpretative hypothesis of the phenomenon.

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Having noted in albinism, whether occurring in the human or animal species, congenital pathological changes associated with and especially located in the visual, auditory and nervous apparatus, we have proposed to check the possible changes in the permeability to sodium fluorescein of the hemolabyrinthine, liquor and ophthalmic barriers in the albino rabbit.

Albinism is a hereditary metabolic change in the melanocyte involving the incapability of synthesizing tyrosinase required for the conversion of tryosine into melanin (A. Kukita, T. B. Fitzpatrick). The grains of this pigment in the melanocyte are not inert particles but active metabolic units containing a heterogeneous mixture of proteins, melano proteins and enzymes. These are, for example, the tyrosinases, succinic dehydrogenase and dopa-oxidase (H. Herman, M. B. Boss). The melanic pigmentation in mammals is assigned to the melanocyte system, an embryological, morphological and biochemical unity derived from the neural crest (J. Stambury, J. B. Wyngaarden, D. S. Fredrickson). The metabolic defect in albinism can involve the whole melanocyte system (universal albinism), the greater part of the melanocytes (generalized albinism) or just one area of distribution of melanocytes (localized albinism). There are many nomenclatures proposed. Localized albinism is also generally termed "leucismus".

* Numbers in the right margin indicate pagination in the original text.

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Genetically, it is the universal form as well as the generalized one which is hereditary as autosomal recessive characteristics. The form localized in the eyes is transmitted according to the recessive mode related to sex. The leucismus follows the laws of dominance (C. Stern).

Albinism in the various types is often associated with other anomalies. It is noteworthy that the albinos are anosmic or hypoosmic owing to the decrease or deficiency of pigment in the olfactory sensory cells. In the same way, the frequent deafness in animals having white fur has been a phenomenon rather well known since the middle of the 18th century (H. Schel, H. Pizibon, D. Wolff, T. G. Wilson, F. Kane).

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According to Turaine, among the pathological correlations of albinism may be found imbecility or idiocy, schizophrenia with or without microcephalia, deafness or hypoacusis as well as various ocular disorders among which is included retinitis pigmentosa. The more important syndromes are those of Waardenburg, Lobstein van der Hoeve, as well as J. Mende. Furthermore, if we consider abiotrophy, according to the concept of Dureux, to be a dysmetabolic genopathy of the cellular enzymatic complex, applied in a limited way to a few systems, we can understand the abiotrophic associations involving other bodily functions and including albinism, tapetum-retinal degenerations and in general disorders related to a genetic defect of the neural crest connected with pigmentary disturbances contributing to make current the problem of melanogenesis and the functional significance of melanin. Thus, owing to the etiopathogenetic embryological unambiguity, we can link albinism to the syndrome of Wogt-Koyanagy as well as to the syndrome of Laurance-Moon-Bardet-Biedel. It is also linked to the associations of pigmentary retinitis and deaf mutism, retinitis with congenital deafness, vestibulocerebellar ataxis and mental disturbances, etc.

As we have set forth, given the concomitance of seats of pathological symptoms which occur more frequently associated (ears, eyes, nervous system, skin, cutaneous appendages) with that of distribution of the melanocytic system, we believe our functional investigation is justified extended to the three systems: We sought to control the permeability of the three barriers. Albino animals were used to show a possible modification in absence of the intracellular enzymatic complexes related to reactions for synthesizing melanin from amino acids (Figure 1).

For our experiment, we used 14 albino rabbits (apparently universal ones) and 14 normochromic control rabbits. These were adult specimens, of both sexes, with weight ranging between 2000 and 2500 g, kept under the same conditions of environment and light. Each pair of a first group of eight albinos was injected with sodium fluorescein into the veins, all doses being 100 mg, 115 mg, 120 mg and 114 mg/kg respectively. The same thing was done to the subjects of a corresponding group of normochromic specimens. These animals were sacrificed one hour after the injection. All the pairs of a second group of six albinos had introduced into their veins 120 mg/kg of the same dye and the same thing was done to the corresponding control group.

The pairs of these two last groups were sacrificed at intervals of 1 h, 3 h and 6 h from time of injection. We also observed in these animals

the time passed between the injection of the dye and its appearance, appreciable with direct view using normal light, in the anterior chamber of the eye. Immediately after death, samples were taken from all animals of liquor, aqueous humor, vitreous humor, perilymph, endolymph and the rate of stain actually present determined by direct comparison with known solutions of fluorescein, with scaled dilutions, evaluating the fluorescence with Wood's light. The values obtained were compared for each group of albinos with those encountered in corresponding normochromic rabbits.

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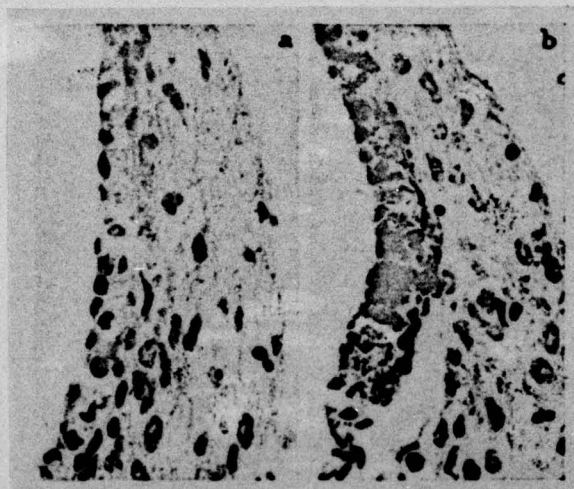


Figure 1. (From: C. Beck. The pigment of the stria vascularis. Archiv f. Ohren, Nasen u. Kehlkopfheilk, 179, 1961, p. 51)

a. Stria vascularis of albino rabbit: melanin absent.

b. Stria vascularis of normochromic rabbit: melanin present.

The approximate average rate of fluorescein encountered in the various liquids examined are listed in the following table (A and B). From analyses of the results, it can be found that such concentrations, whether in albinos or in normochromic animals, have always been found in decreasing order in the aqueous humor, perilymph, endolymph, vitreous humor as well as in the liquor. In the albino rabbit, a minor permeability of the three barriers to fluorescein was seen clearly when raising the relative thresholds. More particularly, the threshold for the labyrinthine liquids was increased for 110 mg/kg (L. Beretta, E. Sacco, G. Galioto, G. Sambuco) to 115 mg/kg.

This decrease in permeability was also seen in the time base of appearance of the stain in the aqueous humor which ranged from 3 min in the normochromic animal to 24 min in the albino. Furthermore, we believe we have encountered a delay in the elimination of the stain from the liquor systems during examination to the extent that, at the sixth hour following injection, the concentration of fluorescein was greatly diminished in the normochromic animals and the rates were more similar to those of the control animals than to the albinos with the exception of the liquor in which, at the sixth hour in the normochromic animals, it was no longer detectable whereas in the albinos there was still found a concentration of $\frac{1}{640,000}$.

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However, we felt we should state a posteriori that the chemical complexes of the chain of transformations from amino acid to the melanic pigment influence the cellular permeability. Indeed, their absence decreases it. In addition, it affects the similar behavior of the three

- A. Summary table of average approximate values of concentrations of fluorescence encountered in albino and normochromic rabbits, one hour following injection of stain. (Animals kept during the experiment in a lighted thermal environment using natural light filtered through glass.)

A) Tabella riassuntiva dei valori medi approssimativi di concentrazione di fluorescenza riscontrati in conigli albini e normocromici dopo 1 ora dall'iniezione del colorante (animali mantenuti durante l'esperimento in ambiente illuminato con luce naturale filtrata da vetri).

Albino = Fluorescin 100 mg/Kg.		Normochromic = Fluorescin 100 mg/Kg.	
Liquor	---	L	---
* Umore Aqueo = 1/640.000	---	U.A. = 1/240.000	P. = ---
** Umore Vitreo = ---	---	U.V. = 1/640.000	E. = ---
Albino = Fluorescin 115 mg/Kg.		Normochromic = Fluorescin 115 mg/Kg.	
L	---	L	---
* U.A. = 1/240.000	P. = 1/320.000	U.A. = 1/500.000	P. = 1/240.000
** U.V. = ---	E. = 1/640.000	U.V. = 1/450.000	E. = 1/300.000
Albino = Fluorescin 120 mg/Kg.		Normochromic = Fluorescin 120 mg/Kg.	
L	---	L	---
* U.A. = 1/160.000	P. = 1/240.000	U.A. = 1/100.000	P. = 1/160.000
** U.V. = 1/500.000	E. = 1/320.000	U.V. = 1/280.000	E. = 1/240.000
Albino = Fluorescin 114 mg/Kg.		Normochromic = Fluorescin 114 mg/Kg.	
L	---	L	---
* U.A. = 1/300.000	P. = ---	U.A. = 1/560.000	P. = 1/290.000
** U.V. = ---	E. = ---	U.V. = 1/200.000	E. = 1/370.000

*Aqueous humor
**Vitreous humor

- B. Summary table of average approximate values of concentrations of fluorescence encountered in albino and normochromic rabbits 1 h, 3 h and 6 h following injection of stain using a dose of 120 mg/kg. (Animals kept during the experiment in an internal illuminated environment using natural light filtered through glass.)

B) Tabella riassuntiva dei valori medi approssimativi di concentrazione di fluorescenza riscontrati in conigli albini e normocromici dopo 1 h., 3 h., 6 h., dall'iniezione del colorante alla dose di 120 mg/Kg. (animali mantenuti durante l'esperimento in ambiente interno illuminato con luce naturale filtrata da vetri).

After Dopo 1 h.		After Dopo 3 h.		After Dopo 6 h.	
Albino		Albino		Albino	
Normochromic		Normochromic		Normochromic	
L	1/410.000	L	1/320.000	L	1/640.000
U.A.	1/160.000	U.A.	1/220.000	U.A.	1/280.000
U.V.	1/370.000	U.V.	1/460.000	U.V.	1/550.000
P.	1/230.000	P.	1/260.000	P.	1/310.000
E.	1/320.000	E.	1/450.000	E.	1/600.000

liquor systems examined coinciding with the frequency of the pathological symptoms observed in association. Consideration should be given the great influence on the melanogenesis of the pituitary gland (intermedin, ACTH) and the neural vegetative system, hence on the hypothalamic centers with all their innumerable connections. Consideration should also be given the influence of luminous retinal stimuli on the hypothalamus, on the pituitary gland and through the latter on the activity of the gonads, on the metabolism of glucides, lipids and on the distribution of the melanic pigment (E. G. Hague, S. Kurotsu-Bathman, C. Sapupp., W. Chavin). This suggests that this latter substance belongs to the melanocytic system and feels the effect of humoral stimulation from the pituitary gland even in the seats not directly exposed to light (ears, leptomeninges, etc.) thus explaining, in addition to the protective action, above all the regulation of permeability of the barrier through reversible enzymatic processes contributing to controlling the daily biorhythm.

On the basis of these elements, taking into account that during pregnancy even as early as the first weeks there is a pituitary gland hyperfunction with hyperpigmentation, we formulate the hypothesis that one part of the so-called sympathetic disorders may be attributed to an increase in the melanocytic regions of the cellular permeability. This would involve an accentuated olfactory sensitivity through variations in the bioelectric potentials of the membrane (Negus) and chemical-physical modifications of the labyrinthine liquids to which can be reconnected in part the etiology of the hyperemesis (V. Tanturri) owing to dysvegetative disorders caused by local above-threshold stimulations. As pregnancy continues, an adaptation would take place with the attenuation and disappearance of the syndrome. To prove hyperosmia of pregnancy, reference can be made to hyperpigmentation of the Schultz cells and the well-known case of the young negro reported by Hutchinson who began at 12 years of age to undergo a progressive depigmentation. Anosmia was noted together with the depigmentation. When he subsequently returned to his normal color, he regained the sense of smell.

Furthermore, it is well known that negroes have a much more sensitive sense of smell than white persons (Ogle) and that albinos are either anosmic or hyperosmic. The fact that melanin or its predecessors play a new physiological role in the cellular oxido-reductive processes is also pointed out by C. H. Sannié who makes reference to many authors who are interested in the argument and who have demonstrated how the acid 5,6 dihydroxyindolo-2-carboxylic quinone which appears in the chemical reaction chain of the melanogenesis is reducible in reverse.

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A concentration of M/1180 triples the rate of respiration of the erythrocytes in rabbits. It has been proven that in crustacea, melanin is always found associated with riboflavin. This tends to demonstrate that both systems have a common role in certain physiological reactions (Sannié).

With regard to what has been stated before, it only remains to conclude that the role of melanin in organisms is still far from being completely understood and represents, for all fields of medicine, a fascinating field for investigations.

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